Allergy Abstracts

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Asthma and Hay Fever

The Development and Management of Intractable Asthma of Childhood. Tuft, H. S.: A. M. A. Am. J. Dis. Child. **93**: 251, 1957.

The case histories of more than 500 children studied at the Jewish National Home for Asthmatic Children in Denver, Colorado, during the past 17 years were reviewed. The children ranged in age from 5 to 16 years and came from all sections of the United States. Approximately 50 per cent of these children lost their asthma within a few days following admission and had no further attacks during their stay. In another 30 per cent there was a decrease in asthma during the first year at the institution, and freedom from symptoms was achieved during the second year. Ten per cent of the children lost their asthma following admission but developed recurrences during the pollen season. In about 10 per cent of the patients, the asthma continued unchanged. Two children died while at the institution.

The factors which might be responsible for the relief attained were reviewed. Climate was quickly ruled out as a significant factor in the over-all

result, since 7 children from the immediate area and 24 from areas with similar climates progressed just as well as those who came from more remote areas. Avoidance of contact with offending allergens was not considered to be a key factor, since many of these patients had previously been kept on similar environmental precautions while being treated at home. The patients were encouraged to eat a full diet, and most of them tolerated this regime well. In the small group that had symptoms were those who were markedly sensitive to egg, fish, or nuts. Following ingestion of the offending foods, these patients usually developed urticaria rather than asthma. Since the Denver area has a rather active mold season and a pollen flora similar to that of areas from which the children came, elimination of air-borne inhalants could not be regarded as a major factor contributing to the patients' improvement.

The importance of separation from the parents as a cause of improvement became evident when it was noticed that some patients developed sudden flare-ups shortly prior to anticipated visits from relatives or prior to vacations or actual discharge to their homes. At the National Home the patients were away from their overprotective and overanxious parents. The last 100 admissions to the institution were given a battery of psychological tests. It was found that children with asthma, as a group, were of average intelligence and tended to show marked immaturity, anxiety about the body, and difficulty in their relationships with their parents and other people. It is suggested that "parentectomy" may be the first step toward rehabilitation of a severely asthmatic patient. R. W.

Status of Corticotropin and the Steroid Hormones in Therapy of Allergic Disease. Bookman, R.: J. A. M. A. **165**: 1950, 1957.

The use of ACTH or the adrenal steroids is indicated in self-limiting types of allergic reactions, such as drug or penicillin sensitivities, and in the small group of patients who either do not respond adequately to accepted allergic measures or who develop isolated refractory episodes of allergic disease. In 699 consecutive cases under specific allergic management, ACTH or steroids were required in only 45 patients. In most of these, short-term therapy was adequate. The long-term use of steroids was resorted to in 9 patients with asthma, all of whom were past the age of 50. Forty per cent of the entire series of patients were under 16 years of age, and only 3 in this age group required hormone therapy. M. C.

A More Direct Liquefaction of Bronchial Secretion by Aerosol Therapy. Levine, E. R.: Dis. Chest **31**: 155, 1957.

Ninety-six patients with severe chronic pulmonary disease were treated with an aerosol which contained Tergitol 08 (sodium 2-ethylhexy sulfate), 0.125 per cent, and potassium iodide, 0.1 per cent, in sterile water. The ages of these patients varied between 6 and 70 years; more than half were over 40. In this group, 34 had bronchiectasis, 27 had asthma, 22 had emphysema, and 13 had other forms of chronic lung disease. When the patients were analyzed by disease combinations, 16 were found to have asthma and chronic bronchitis, 10 had asthma and bronchiectasis, and 9 had asthma and emphysema. Treatment was administered in most cases for one-half hour 4 times a day and was combined with intermittent positive pressure breathing. Patients received this therapy for from one week to 6 months. When the findings were analyzed in terms of liquefaction of sputum and ease of expectoration, it was found that excellent results were achieved in 66 cases and good results in 5.

No evidence of tracheobronchial irritation, iodism, changes in the blood count, or pathologic findings in the urine were encountered. It was concluded that this aerosol solution appeared to be definitely beneficial in bronchopulmonary disease with thick viscous mucopurulent secretion. E. W.

The Bronchodilator Effect of Compound 20025 (1-0-Chlorophenyl-2-Isopropylaminolthanal Hydrochloride). Johnston, R. E., and Shipley, R. E.: Am. J. M. Sc. **233**: 303, 1957.

The effect of Compound 20025 (Isoprophenamine) as a bronchial dilator was studied in 34 patients with severe asthma. Compound 20025 was given orally in doses of 20 to 40 mg. at intervals ranging from 4 to 8 hours. Some of the patients were kept on the medication for periods varying from 2 to 9 months. Several severe asthmatics were studied in the hospital.

Compound 20025 was found to be a very effective bronchodilator and increased both the vital capacity and the maximum expiratory flow rate (MEFR) for a period of from 2.5 to 8 hours following a single dose. When prolonged therapy was desired, 20 to 40 mg. of medication was given 4 times a day. By vital capacity and MEFR studies, Compound 20025 was found to be more beneficial than other bronchodilators. The medication produced central nervous system stimulation in almost all patients to some degree. The patients developed fine or coarse tremors, inability to sleep, and increased restlessness. After a few days on the drug, these symptoms tended to diminish. Amytal given with Isoprophenamine tended to reduce the objectional side effects. The amount of Amytal given was approximately two-thirds of or equal to the Isoprophenamine dosage. After prolonged administration, there was no alteration in blood count, urinalysis, blood urea nitrogen, serum glutamic oxalacetic transaminase, PSP excretion, liver function, blood pressure, or electrocardiogram. R. W.

Aminophylline Toxicity. Soifer, H.: J. Pediat. **50**: 657, 1957.

Toxic reactions to aminophylline suppositories occurred in 37 pediatric patients with respiratory ailments. The major toxic symptoms were restlessness, repeated vomiting, fever, and convulsions. Eleven patients died. The only therapeutic measures employed were supportive. It is suggested that a safe dose of aminophylline in suppository form is 5 mg. per kilogram of body weight every 8 hours and that suppositories in 50 mg. and 100 mg. strengths should be made available in order to decrease the possibility of overdosage. The incorporation of ephedrine into the medication appeared to be contraindicated. M. C.

Long-Term Treatment of Bronchial Asthma by Steroids and Promotion of Psychological Security. Peket, L., Nissimow, N., and deVries, A.: Harefuah **53**: 144, 1957.

Eighty-eight asthmatic patients, ranging in age from 9 to 49 years, were observed for periods of 6 to 27 months. All but four had developed asthma after immigrating to Israel and most of them had their symptoms within five years after their arrival. Fifty-two patients had had symptoms for two years or less. Twenty-nine patients had had one or more previous hospital admissions. During the study, the treatment consisted of the administration of antibiotics whenever there was a respiratory infection, avoidance of contact with offending allergens, promotion of psychological security, and administration of

steroids when the aforementioned measures or placebos were ineffective. Each patient was assigned to one of the physicians on the ward with whom he established a personal contact. He was seen in the clinic regularly or whenever the necessity arose. Admission to the ward was assured whenever requested. All cases were studied by a social worker. In the less severe cases, patients were given a placebo instead of steroids. Prolonged hormonal treatment consisted of either cortisone or Meticorten in maintenance doses with ACTH gel at intervals of from 3 to 6 months. Some patients received only ACTH gel.

Eight patients were favorably affected by steroids and required them only during special seasons. The results of prolonged maintenance on steroid therapy were good in 77 cases; 28 of the 77 patients had been given placebo ineffectively for about a month. Only three patients failed to benefit at all from cortisone, up to 3 mg. daily for several months. The efficacy of long-term treatment with steroids could be determined only by trial. I. G.

Etiology and Pathogenesis of So-called Bakers' Asthma and Millers' Asthma. Klunker, V. W.: Schweiz. med. Wchnschr. **87**: 714, 1957.

In a study of 15 bakers and 8 millers with bronchial asthma, it was found that flour was the usual etiological agent in the bakers. In this group rhinitis accompanied and usually preceded the asthma, and skin reactions were positive in most cases. In a few bakers, skin reactions were negative and the asthma was regarded as having developed as a result of a chronic dust-induced bronchitis. In millers with asthma, reactions to cutaneous tests were usually negative and allergic factors appeared to play no causal role in most cases. Instead, degenerative changes in the lungs, leading to chronic bronchitis, asthma, or emphysema, appeared to be due to a mechanical action by dust. Rhinitis was usually absent. This study indicated that the cause of asthma in bakers and millers differed, although in both groups the disorders were of occupational origin. M. C.

First Therapeutic Experiences With Prednisolone Hemisuccinate Given Intravenously to Patients With Bronchial Asthma. Sicuteri, F., and Ficini, M.: LaSettimana Medica **44**: 606, 1956.

A dose of 25 mg. of prednisolone hemisuccinate was given intravenously one or more times daily to 10 patients with bronchial asthma. A complete remission of symptoms was observed in 8 patients, and marked improvement was noted in the remaining two. The maximum response usually occurred within 21 to 24 hours after therapy was instituted. In 4 patients, the effect of the treatment was maintained by oral administration of prednisolone. In the remaining patients, symptoms reappeared in a mild form after treatment was ended. Whenever the treatment was repeated, a remission of symptoms resulted. There were no harmful effects from the therapy. M. C.

Otorhinology and Ophthalmology

Heart and Moisture Exchange of Respiratory Mucous Membrane. Cramer, I. I.: Ann. Otol., Rhin. & Laryng. **66**: 327, 1957.

The apparatus employed in these studies for the measurement of heat and moisture exchange is described in detail. Air samples were collected from subjects while they were kept in air-conditioned rooms in which temperature and humidity could be accurately controlled. Inspiratory and expiratory samples were obtained from the posterior choana of a normal subject and

from the trachea of a patient who had had a laryngectomy. Another study was done on a glass tracheal model that had the dimensions of an "average" adult trachea; the model was lined with blotting paper saturated with distilled water and was warmed by an encircling heating element. This model was placed at the mouth of the subject, and air samples were obtained from the end of the glass tube close to the lips. The subjects were studied at dry bulb temperatures of 51° F., 72° F., and 80° F. with relative humidities of 65, 45, and 25 per cent, respectively.

Air which contained 52 grains of moisture per pound of dry air at 72° F. extracted an additional 123 grains from the trachea and was warmed to 85° F. when it passed directly over the mucous membrane. The tracheal model heated to 85° F. yielded the same amount of moisture. These figures were similar to those obtained with the posterior choana air samples which had passed through the nose. When inspired air was 51° F., the trachea raised the temperature to 84° F. while the nasal mucosa increased the temperature to 89° F. At 51° F., the moisture was increased only slightly more by the nasal mucosa than by the trachea or the tracheal model. Comparative studies at 80° F. and 25 per cent relative humidity again revealed only minimal differences between the values obtained with air samples from the nasal or tracheal mucosa or from the tracheal model.

The results of these studies indicate that the trachea and even the tracheal model are as efficient in conditioning air for pulmonary gas exchange as is the nose. The author suggests that the nasal mucous membrane is primarily concerned with body heat regulation and only secondarily with air conditioning.

B. S.

Provocative X-ray Therapy as a New Aid to the Diagnosis of Suspected Sinusitis. Swineford, O., Jr., Cooper, G., Jr., and Pearsall, H. R.: Ann. Allergy **15**: 293, 1957.

Asthma and certain chronic nasal conditions frequently are closely associated with infections of the paranasal sinuses. Although the diagnosis of infected sinuses is usually a simple matter, it is not always possible to obtain confirmation by any of the conventional procedures. In such cases, a provocative dose of x-ray can provide the means of establishing the diagnosis. It has been observed that a therapeutic dose of 200 r can provoke a purulent nasal discharge and definite exacerbation of such symptoms as hay fever, asthma, cough, headache, or malaise.

In a series of 40 patients in whom sinus infection was suspected but unestablished by the usual rhinologic and roentgenologic examinations, provocative x-ray treatment confirmed the diagnosis in 15 instances. Nine of these 15 patients were relieved of their major complaints when the sinus infection was cleared.

H. F.

Miscellaneous Allergies

Clinical Use of Prednisone and Prednisolone in Allergic States and Collagen Diseases. Gregoire, G., and Rose, G.: Canad. M. A. J. **77**: 833, 1957.

The authors treated 146 patients with prednisone and prednisolone. Each of the drugs was used separately and also in combination with other medicaments. One compound contained 5 mg. of prednisone, 2 mg. of Chlor-Trimeton, and 75 mg. of ascorbic acid; another contained 5 mg. of prednisolone and 4 mg. of carbinoxamine maleate. Patients in all age groups with collagen diseases and with the more common allergic conditions were included in this study. The dose of the steroid varied from 5 mg. to 150 mg. daily.

The results obtained in hay fever and asthma were quite good. One asthmatic patient required as much as 180 mg. of prednisone in 24 hours before relief was obtained. The dosage was then gradually reduced as the patient's condition warranted it. Two asthmatic patients failed to respond to 40 mg. a day, even though the medication was maintained at this level for as long as three weeks. Another asthmatic patient was refractory to this type of therapy. He had previously failed to respond to treatment with ACTH, cortisone, and hydrocortisone. Even on 30 mg. a day, many patients required additional medication, such as Adrenalin or aminophylline, in order to obtain complete relief. Most of the patients remained free of symptoms for from 2 to 10 days following withdrawal of the steroids, after which their symptoms gradually reappeared. A few experienced remissions that lasted as long as six months. Patients with urticaria and angioedema did not respond as well as those with respiratory allergy.

At least 25 per cent of the entire group had no relief and actually felt better when not receiving steroids. Fifty patients had received either corticotrophin, cortisone, or hydrocortone prior to the present study. Of these, 33 were both objectively and subjectively better on the present regime and almost all preferred prednisone to the previous compounds. The remaining 17 patients in this group were not helped by either prednisone or prednisolone. No essential difference was noted between the benefits afforded by prednisone or prednisolone. Although the side effects from steroids were minimal, it is suggested that antihistamines be used in the routine treatment of hay fever and that steroids be reserved for use only in the treatment of resistent cases.

R. W.

Intestinal Obstruction—A Heretofore Undescribed Visceral Manifestation of Allergy to Penicillin. Bassett, A. A., and Cole, L. J.: Canad. M. A. J. **77**: 588, 1957.

A 64-year-old man with a foot injury was given 600,000 units of procaine penicillin on three successive days. Two weeks later he developed generalized urticaria which was not relieved by antihistamines. Within another week he developed generalized erythema multiforme complicated by bullous and hemorrhagic lesions. After treatment with local applications and with oral prednisone, the skin lesions slowly subsided during the following three weeks. When the hemorrhagic eruption was at its peak, the patient complained of abdominal pain, nausea, and diarrhea. When steroid therapy was discontinued, the diarrhea stopped; constipation developed and was accompanied by vomiting, abdominal distention, and severe cramps. The patient was eventually hospitalized. At this time the abdomen was moderately distended and extremely tender. There had been no evidence of any bowel activity for at least 48 hours.

A laparotomy was performed and an obstuction was found in the proximal segment of the jejunum. Almost the entire small bowel mesentery was edematous and covered with ecchymotic areas. The biopsy revealed numerous plasma cells in the lamina propria, but only occasional eosinophils were seen. The submucosa showed a very loose and edematous stroma infiltrated with round cells. The blood vessels were dilated and congested.

Normal bowel function returned by the seventh postoperative day. The patient made a complete recovery and was discharged from the hospital nine weeks following the original injury. The author suggests that drug allergy may also be a cause of acute abdominal disease.

R. W.

Thrombohemolytic Thrombocytopenic Purpura With Lupus Erythematosus. Siegel, B. M., Friedman, I. A., Kessler, S., and Schwartz, S. O.: Ann. Int. Med. **47**: 1022, 1957.

Thrombohemolytic thrombocytopenic purpura is a syndrome often referred to as Moschcowitz's disease and characterized by the association of hemolytic anemia, thrombocytopenia, and bizarre neurological manifestations. The condition appears to be related to the collagen diseases, and in a number of reported cases a high incidence of allergic phenomena has been noted. In the present case, the triad of signs and symptoms was associated with the presence of the L.E. phenomenon. The patient was critically ill, and treatment with ACTH and cortisone brought about an improvement in the blood picture but did not otherwise affect the condition. Splenectomy was followed by marked improvement in the symptomatology. H. F.

Reactions From Multiple Injections of Benzathine Penicillin G. Sherwood, R. W., Gronbeck, C., and Denny, F. W., Jr.: J. A. M. A. **165**: 667, 1957.

The incidence and severity of reactions after repeated intramuscular injections of benzathine penicillin G (Bicillin) was studied in an army unit. Patients with definite histories of allergic reactions to penicillin were excluded from this study. One group of 1,567 subjects received 600,000 units every four weeks; the other group of 1,708 men received 900,000 units every six weeks. No immediate shock reactions occurred, but during the six months of the study 16 men were hospitalized because of urticaria, angioneurotic edema, or joint symptoms. Eleven were hospitalized after the first injection, 4 after the second, and one after the third. Usually all symptoms and signs disappeared within three days after the initiation of treatment; one patient was hospitalized for 40 days because of recurring urticaria. The "cumulative probability of reacting" was approximately 6 per cent in each of the two groups. "When those with reactions were excluded the probability of reaction decreased markedly after the first injection, and prolonging the interval between injections did not change the reaction rates. It was concluded that the use of repeated intramuscular injections of benzathine penicillin G was a feasible and safe procedure." M. C.

Milk Allergy—Diagnostic Aspects and the Role of Milk Substitutes. Fries, J. H.: J. A. M. A. **165**: 1542, 1957.

The author found that 5 per cent of his patients described symptoms which could be attributed to milk. After detailed allergic investigation, he discovered that the actual incidence of milk allergy was less than 0.3 per cent. He noted that many symptoms which could not be attributed to allergy to cow's milk were caused by nonantigenic components of the milk, special toxins, certain physical properties, poor preparation, or bacterial contamination. Since sensitization to milk is usually due to the lactalbumin fraction, a substitute product in which this protein is altered is recommended. Mammalian-derived milk seemed preferable to vegetable milks for maintaining nutrition. M. C.

Severe Immediate Reactions to Biologicals Caused by Silk Allergy. Brown, S. F., and Coleman, M.: J. A. M. A. **165**: 2178, 1957.

Three patients with atopic histories, ranging in age from 8 to 12 years, were reported to have experienced severe immediate allergic reactions following the injection of one or more of the following preparations: tetanus toxoid

(fluid), tetanus toxoid (aluminum phosphate adsorbed), triple antigen (aluminum phosphate adsorbed), human gamma globulin, and typhoid-paratyphoid vaccine. Each of these three patients gave a positive direct or passive transfer reaction to silk, and all of the aforementioned agents were products of Company A. Passive transfer sites showed no response to similar biologic agents produced by other pharmaceutical companies or to potassium penicillin G, beef extract, and buffered saline. As a control, passive transfer tests were done with all of the above substances on sites sensitized with sera obtained from two patients allergic to pollen and foods. No positive reactions were obtained. It is known that each of the biological agents produced by Company A which the above patients received had been filtered through silk during the manufacturing process. Previous instances have been reported in which allergic reactions to Company A's products were traced to their silk content. Apparently, sufficient amounts of silk antigen became incorporated into the biological products to cause severe reactions in silk-sensitive patients. The authors point out that other allergic reactions that have been attributed to other biological agents may have been caused by silk. T. Chao.

Survey of Human Allergy to North American Snake Venoms. Parrish, H. M.: Arizona Med. **14**: 461, 1957.

Scratch tests with fresh undiluted cottonmouth moccasin and eastern diamondback rattlesnake venoms were performed on 30 patients who had been bitten previously by pit vipers. Sixteen of this group were professional herpetologists. Positive reactions were obtained in 7 of the 30 persons tested. Positive passive transfer reactions were obtained with sera obtained from those patients. Similar tests were done on 20 persons with no previous exposure to snakebite. These were all negative. There was evidence of cross sensitivity between the two snake venoms tested. The incidence of positive skin test reactions was not significantly different in patients who had previously been bitten once and those who had been bitten more than once. The possibility exists that fatal anaphylactic reactions may occur in persons with previous envenomization when they are bitten again. M. C.

Clinical and Biological Studies on Schönlein-Henoch Syndrome. Bernard, J., Mathé, G., and Israel, L.: Presse méd. **65**: 759, 1957.

Fifty-one patients with the Schönlein-Henoch syndrome were studied. There was no evidence of the presence of antierythrocyte, antileukocyte, or antiplatelet antibodies in any of the sera. All the sera had capillary toxic properties (different from Forssman antibodies) as demonstrated by the production of local ecchymosis when they were injected intradermally into guinea pigs. These serum properties were also found in some other diseases and in 24 of 140 normal persons. The authors base their suggestion that the capillary toxic factor is an antibody on the fact that it is similar to the factor found in the serum of rabbits immunized against endothelium of guinea pig, that it forms part of the gamma globulin fraction, and that it acts in the presence of complement. It is stressed that many workers have induced the Schönlein-Henoch syndrome experimentally by an immunologic process and that others have demonstrated an "antivascular" antibody by the precipitation technique.

Three varieties of the syndrome are discussed. The first type, described as allergic inflammatory purpura (12 patients), consisted of polymorphic lesions associated with nonhemorrhagic allergic manifestations and a positive family history. From the history, inhalants and foods were suspected as

etiological factors and confirmatory positive (sometimes hemorrhagic) skin reactions were demonstrated. The second type is designated as acute idiopathic inflammatory purpura (25 patients); it occurred only in children, exclusively petechial, and was influenced by posture. The third type, described as chronic inflammatory purpura (24 patients), appeared in adults and was characterized by chronicity or frequent recurrences, by the severity of renal pathology, and by a constant elevated gamma globulin. I. G.

Fatal Intolerance to Penicillin. Cecchini, M., and Ferretti, P.: Presse méd. **65**: 254, 1957.

A 40-year-old woman with chronic asthma developed a severe reaction when she was given an intramuscular injection of penicillin following a myomectomy. The symptoms consisted of dyspnea, cyanosis, and tachycardia. She had had a similar but milder reaction two years previously following a penicillin injection. Some time later she was advised to have penicillin and ephedrine by inhalation for relief of her asthma. Upon entering the room where the aerosol was being administered, she became weak, developed cyanosis, severe dyspnea, tachycardia, and hypotension, and became semiconscious. Three days later, when she seemed quite well, she was skin-tested intracutaneously with a penicillin solution. She died within one minute, apparently in anaphylactic shock. I. G.

Anaphylaxis

Hematocrit Changes as Indication of Anaphylactic Shock in the Mouse. Fulton, J. D., Harris, W. E., and Craft, C. E.: Proc. Soc. Exper. Biol. & Med. **95**: 625, 1957.

Female Swiss-Webster mice were sensitized with two intravenous injections of 0.25 ml. standardized antigen preparations consisting of either alum-precipitated bovine serum albumin with *Hemophilus pertussis* vaccine (APBA + HPV) or alum-precipitated bovine serum albumin alone (APBA). Twelve days later, both groups of mice were challenged with 0.25 ml. of APBA injected into the caudal vein. Saline controls were run with both the sensitizing and the challenging injections. Microhematocrits were determined on blood samples from the severed tail of thei mmobilized mouse. Prechallenge hematocrits were calculated to have a maximal variation of 3 per cent. Postchallenge increases of 5 per cent or more were arbitrarily selected as significant.

Although the results vary somewhat with the sensitizing procedure employed, the figures indicate that the incidence of significant hematocrit increase is higher than the death rate. In the test group in which 47 per cent of the animals died in anaphylaxis, 75 per cent showed an increase in hematocrit of 5 per cent or more. Control animals showed a consistent decrease in hematocrit. It is suggested that hemoconcentration may be a means of quantitating sublethal anaphylaxis in the mouse. H. Stryker.

Pharmacology, Physiology, and Pathology

Sensitivity of Respiratory Center to Carbon Dioxide in Emphysema and Cor Pulmonale: Effects of Carbon Anhydrase Inhibition. Taquini, A. C., Roncoroni, A. J., Aramendía, P., and Ros, A. M.: Am. Heart J. **54**: 319, 1957.

Four normal adults and seven emphysematous patients, one of whom was in acute respiratory acidosis and heart failure, were studied. Expired air and

blood from the femoral or brachial artery were analyzed for CO_2 and O_2 content. Oxygen capacity and CO_2 combining power of the blood were measured. Readings were made before and after the inhalation of 5 per cent CO_2 in air or oxygen and were repeated following the administration of acetazoleamide (Diamox) in doses of 12 to 15 mg. per kilogram per day for 2 to 15 days. It was found that Diamox increased total and alveolar ventilation in all but one normal subject and decreased their oxygen consumption and their CO_2 elimination. Their blood bicarbonates decreased and the average arterial P_{CO_2} fell 7 mm. Hg. Blood pH was lowered. When these subjects were then exposed to CO_2 inhalation, ventilation increased 3.8 times over resting values. Prior to Diamox therapy, they had shown an increase of only 2.7 times in resting total ventilation and 2.9 times greater alveolar ventilation when stimulated by CO_2.

Emphysematous patients, when stimulated with CO_2, showed an average of only 54 per cent increase in total ventilation and 82 per cent increase in alveolar ventilation. Their arterial oxygen saturation increased but did not approach normal values. The P_{CO_2}, however, also increased, producing a further lowering of the blood pH. On the inhalation of "pure" oxygen, these patients characteristically developed a fall in total and alveolar ventilation with a sharp rise in arterial CO_2 and a fall in pH. Following the administration of Diamox, total ventilation was unchanged, alveolar ventilation was increased 15.7 per cent over control, arterial P_{CO_2} decreased 6.8 mm. Hg on the average (except for one case of acute acidosis), blood bicarbonates fell 17 volume per cent, and pH was lowered 0.07 units. Excluding 2 cases of acute anoxia, there was a 9.7 per cent increase in oxygen saturation. These subjects then were exposed to CO_2 and showed improved responsiveness over their control (untreated) responses. It is concluded that in chronic acidosis Diamox may be useful. The use of this drug in acute acidosis introduces the danger of intensifying the acidosis and is justified only if hyperventilation is obtained. The basis for the lessened ventilatory response to carbon dioxide by emphysema patients is not chronic anoxia, mechanical impairment to airflow, or changes in blood buffering power; rather it is due to acclimatization to CO_2 itself. E. K.

Pulmonary Changes in Collagen Diseases. Kuzma, J. F.: Dis. Chest **32**: 265, 1957.

In collagen diseases, the initial precipitation of acid mucopolysaccharides is followed by cellular reaction. Examination of loose connective tissue may show considerable intercellular ground substance. In other areas there is development of vacuoles, as well as some swelling and separation of the delicate fibriles; moreover, there is actual precipitation and appearance of granular density. In large blood vessels, the elastic lamina may disappear and are replaced by a swollen, edematous, vacuolated tissue. Eventually these vessels may collapse. These changes have been referred to as fibrinoid necrosis. In addition to the connective tissue and vascular changes previously described in the alveolar walls, there are foci of widening and increased cellularity. These areas constitute points of fibrinoid necrosis. There is disruption of the alveolar wall, widening, smudginess, cellular reaction, and evidence of leakage. These changes are followed by rather severe proliferation of the alveolar lining cells and organization of fibrin exudate within the alveolar spaces. At this stage, the lung is described as "carnified." The organization of fibrinoid necrosis of alveolar walls is at times attended by large histiocytic cells, some of which suggest features of an Aschoff nodule. At this stage of the disease,

the gross appearance of the lung is one of mottled hemorrhages, considerable increase of consistency, and very fine granularity. Within days or weeks, the process undergoes resolution, and there is condensation of the ground substance of involved areas and accentuation of all connective tissue zones which have been involved. The inflammatory cellular response gradually disappears, and a marked thickening of the alveolar walls can be observed. Eventually, there is a rather dense alveolar wall pattern outlining very irregular air spaces. The breakdown of alveolar septa and the formation of irregular air cells lead to the formation of cysts. In acute rheumatic fever, lupus erythematosus, and polyarteritis, the acute and subacute patterns described are encountered. In rheumatoid arthritis, dermatomyositis, and especially in scleroderma, the progress of the change takes place much more slowly and the earlier stages of fibrinoid necrosis frequently are not significant. Since such diseases have recurrences and exacerbations, much of the lung may eventually become involved and the result may be an indurated, rubbery, dark, hypocrepitant lung (rheumatic fever, disseminated lupus) or one of cystic pattern (scleroderma especially). E. W.

The Use of Noscapine (Narcotine) as an Antitussive Agent. Segal, M. S., Goldstein, M. M., and Attinger, E. O.: Dis. Chest. **32**: 305, 1957.

Next to morphine, Noscapine is the second most abundant alkaloid of opium. It is an isoquinoline derivative, related to papaverine. It is rapidly absorbed after oral or parenteral administration, it disappears rapidly from the blood stream, and it appears only in traces in the urine. Its fate is unknown. It has been reported that it is the least toxic of the opium alkaloids in mice, rats, and man. Fifty-one patients with cough due to various types of pulmonary diseases (including acute bronchitis of the allergic and nonallergic types, tracheobronchitis, chronic bronchial asthma, chronic pulmonary emphysema, bronchiectasis, and pulmonary neoplasms) were placed on a program of Noscapine therapy in an attempt to evaluate its effectiveness as an antitussive agent. In this group there were 27 women and 24 men, whose ages ranged from 17 to 75 years. The duration of the cough varied from one week to 30 years. The dosage of Noscapine varied from a single dose of 15 to 30 mg. at bedtime to 15 to 60 mg. 2 to 6 times daily. In fifty (94 per cent) out of 54 trials with this drug in 51 patients, beneficial effects were noted. Pronounced suppression occurred in 26 trials in the group (48 per cent). A comparison of the relative effectiveness of Noscapine with dihydrocodeinone, X-71, codeine, Dilaudid, and Hydryllin revealed less effectiveness in 7 of 30 trials, no change in 9 of 30 trials, and significant improvement in 14 of 30 trials. Side effects were few, but drowsiness was noted in 3 patients, difficulty in raising secretions in 2, and headache in 1. A gradual loss of effectiveness was observed in 3. E. W.

A Case of Polyarteritis Nodosa With Multiple Infarcts in the Lungs. Sochocky, S.: Dis. Chest **32**: 335, 1957.

Polyarteritis nodosa, with multiple infarcts in the lungs, was observed in a 51-year-old white man who had had recurrent pneumonic infections for a 3-week period prior to admission to the hospital. X-rays showed rounded opacities in the upper parts of both lung fields and fluid at the left base. Treatment with antibiotics failed to improve the patient's condition. Roentgenograms taken 2 weeks later showed rounded opacities scattered throughout the right lung and in the left upper lung field with fluid at the right base.

Cultures of the aspirated fluid were reported as negative. The blood count on admission showed 16,000 white cells with 7 per cent eosinophils. Urinalysis revealed a low specific gravity with some albumin and some red cells and casts. Bronchoscopy failed to reveal any abnormality. The patient expired approximately 2 months after the onset of his illness. Post-mortem examination revealed a number of well-defined, grayish white to creamy yellow ovoid or spherical nodules. These nodules consisted of necrotic, eosinophilic material surrounded by granulation tissue and denser fibrous connective tissue; they were probably partially organized infarcts. A partially organized fibrinous exudate was present on the pleural surfaces over the nodules and to a lesser extent elsewhere. The alveolar walls in the lung tissue around the infarcts were often thickened by fibrinous connective tissue. There were scattered areas of bronchopneumonia throughout the lungs. Infarcts were also found in the myocardium, kidneys, adrenals, spleen, and testes. E. W.

Experimental Hypothermia and Allergy. Vukobratovic, S., and Bata, A.: Presse méd. **65**: 7, 1957.

Rats were immersed in ice water at 0° C. to lower their rectal temperature to 14 to 16° C. This hypothermia lasted for about one hour after they were removed from the bath. They were injected intraperitoneally with a solution of dextran (a histamine liberator) and were observed for two hours. The anaphylactic phenomena usually seen after dextran administration (cyanosis and edema of extremities, hemoconcentration, mild hypothermia, and arterial hypotension) did not appear in the refrigerated animals. The average level of histamine in the plasma, as measured by the isolated guinea pig intestinal strip method 30 to 45 minutes after the injection, was 175 meg. per liter. In nonrefrigerated control animals the level rose to 360 meg. per liter, which is about 30 times the level observed in noninjected normal rats. Refrigerated rats were injected intracutaneously with dextran, and soon afterward they were injected intracardially with trypan blue. No discoloration appeared at the skin injection site, in contrast to the intense discoloration in nonrefrigerated animals.

The temperature of the medial aspect of the forearm of 30 asthmatic patients with positive skin reactions to inhalants was lowered to 10° C. by the application of ice cubes. The reactions to intracutaneous tests with the inhalants and histamine were negative, but reactions appeared as the local temperature rose to the normal level of 33° C. The local skin temperature of five patients with friction urticaria was lowered to 5° C. Injection of histamine intracutaneously gave no reaction, but a reaction appeared as the skin temperature rose to 10 to 15° C. The authors conclude that endogenous histamine was not liberated during hypothermia and that local hypothermia prevented the reaction of allergens and histamine except in cases of friction urticaria.

I. G.

Immunology

The Significance of Bacterial Hypersensitivity in Human Brucellosis: Studies on Infection Due to Strain 19 Brucella Abortis. Spink, W. W.: Ann. Int. Med. **47**: 861, 1957.

An excellent opportunity to study the role which bacterial hypersensitivity plays in infectious diseases was afforded when 4 veterinarians were accidentally inoculated with suspensions of strain 19 *Brucella abortis,* which is a stable variant of the organism with attenuated virulence for animals and man. This

strain is a good antigen and is used to immunize cattle against Bang's disease. Prior to the accidental infection, 2 of the 4 patients had not had brucellosis, and brucella agglutinins were not present in their blood. Each was accidentally inoculated intraocularly with a suspension of living strain 19 organisms. The first patient remained asymptomatic for 7 days following the exposure. On the eighth day he developed symptoms, and on the eleventh day he was hospitalized. Strain 19 was isolated from his blood stream on the twelfth day. The serum brucella agglutinin titer was 1-320. An intracutaneous test with the brucella antigen was negative. Prompt recovery followed appropriate treatment. The second patient showed no signs until the tenth day after exposure and thereafter followed the same course and presented hematologic and immunologic findings similar to those found in Case 1, except that the brucella skin test done on the twenty-fifth day produced chills, fever, sweats, and headache.

The other 2 patients were known to have had brucellosis previously and the presence of brucella agglutinins in their blood had been demonstrated. These veterinarians were accidentally inoculated through the skin with the strain 19 organism. In both cases local and systemic symptoms appeared within from 30 minutes to a few hours. Blood cultures remained sterile but brucella agglutinins were demonstrated. It was therefore concluded that the development of immediate or delayed systemic reactions is dependent upon the presence or absence of brucella hypersensitivity at the time of infection. The clinical course in the 4 patients was not unlike that observed in serum sickness, but it is important to remember that acquired hypersensitivity of the delayed tuberculin type is significant in brucellosis, whereas in serum sickness the sensitized person may also exhibit the immediate type of anaphylactic reaction which is associated with circulating or humoral antibodies. Further evidence of acquired brucella hypersensitivity can be demonstrated during the acute phase of the illness by means of a skin test with the brucella antigen and by the flare-up of symptoms when the antigen is introduced into the blood. In experimental animals and in man, reinfection is followed by an explosive inflammatory reaction at the portal of entry. This reaction can be induced with nonviable as well as with living organisms. Nonsensitive persons who have blood stream invasion may exhibit no clinical evidence of this, or in other cases they may show symptoms only after a long period of time. The immediate or delayed appearance of symptoms can be directly associated with the presence or absence of tissue hypersensitivity.

In studies pertaining to the role of the brucella endotoxin in the production of the disease, it was observed that the endotoxin of attenuated brucella caused as much reaction as that from highly invasive forms and it was concluded that this was based on the development of hypersensitivity to the endotoxin. It has also been demonstrated that a direct parallel exists between the toxicity of the endotoxin, when given intravenously, and the results of brucellergin skin tests. "Persons displaying marked dermal hypersensitivity had severe reactions from corresponding amounts of endotoxin given intravenously." The occasional case in which severe brucellosis is accompanied by a negative skin test reaction to the brucella antigen reveals a state of anergy analogous to that of the patient with miliary tuberculosis who fails to react to tuberculin.

It is now generally accepted that a relative immunity against reinfection with brucella is established in animals and in man following infection. However, chronically infected mice have been found to be less tolerant to endotoxin than uninfected controls. This reduction in tolerance is believed to be due to the establishment of hypersensitivity to brucella antigen.

Steroids and corticotropin can control the systemic and dermal effects of brucella antigen and protect adrenalectomized mice against the endotoxin. Patients acutely ill with brucellosis are promptly relieved by the use of steroids.
H. F.

Quantitative Aspects of Antibody Responses of Transferred Lymph Node and Peritoneal Exudate Cells. Dixon, F. J., Roberts, J. C., and Weigle, W. O.: Federation Proc. **16**: 649, 1957.

Accurately definable cell populations were studied with reference to their immunologic and morphologic behavior on transfer to recipient animals. Donor albino rabbits were sensitized with intravenous and subcutaneous injections totaling approximately 250 mg. of bovine serum albumin (BSA) over a period of one month. Cells were obtained from the mesenteric and popliteal lymph nodes (88 per cent lymphocytes) and from peritoneal exudate secondary to the instillation of mineral oil (71 per cent macrophages). Total and differential cell counts and viability determinations were made. In typical experiments, approximately 0.5 billion lymph node or peritoneal exudate cells were injected intramuscularly and subcutaneously into the ventral abdominal wall of recipient x-radiated albino rabbits. The recipients were then stimulated with 1.5 mg. BSA.

Both lymph node and peritoneal exudate cells produced remarkably similar secondary antibody responses. The induction periods were short, and the antigen was eliminated from the circulation within approximately five days. Maximal precipitin titers were found 3 to 4 days after the elimination of the antigen. For every cell transferred, approximately 200 million molecules of anti-BSA were circulating 8 to 9 days later. The antibody present in the recipient on the eighth day probably represents approximately one-third to one-half of the total antibody produced up to that time. In the most successful experiments the transferred cells effected the synthesis of more than twice their own net weight in antibody within eight days. While it is not certain which cells are responsible for antibody synthesis, the major cell types in each population seemed to be primarily involved in the antibody production. Lymphocytes, for example, equal to or greater in number than those present in the peritoneal exudate, where they represent less than 15 per cent of the total cell population, were not able to produce detectable antibody synthesis. The same held true for the macrophages, which represented not more than 8 per cent of the lymph node cell population. Despite the fact that different cells seemed to be producing the antibodies in the two types of transfer, no immunochemical or biologic differences in the antibodies produced were detectable. The quantity of antibody formed suggests that in the intact animal a very small proportion of the total lymphoid tissue might be responsible for sizable antibody production.

Histologic observation of the transfer sites at various intervals throughout the response revealed remarkable similarities in cell development at both lymph node and peritoneal exudate sites. With each suspension the number of recognizable transfer cells decreased within 3 to 6 days and plasma cells appeared throughout the injection sites. The amount of antibody formed could be correlated with the plasma cell population of the sites. This is in agreement with the common belief that the various morphologic entities in the reticuloendothelial system are closely related.
H. Stryker.

Investigation on the Occurrence of Blood Group Antigens in Spermatozoa From Man, and Serological Demonstration of the Segregation of Characters. Preliminary Report. Gullbring, B.: Acta med. scandinav. **159**: 3, 1957.

Washed human spermatozoa were incubated with blood sera from different blood groups. They were then rewashed and incubated with suspensions of various types of red cells. Under these conditions it was shown that certain spermatozoa bind red cell antisera and agglutinate with red cells. Antigens A and B have been found on spermatozoa from a group A B blood type donor. Using enzyme-treated red cells, D antigen in the Rh system has been identified in spermatozoa taken from a blood group O Rh-positive donor. E. K.

Miscellaneous

Tuberculin Testing of the Aged. Chesrow, E. J., and Novak, J. B.: Dis. Chest **32**: 217, 1957.

Two thousand one hundred four persons of advanced age were skin-tested by the intradermal method of Mantoux, using 0.1 mg. of Old Tuberculin. More than two-thirds of this group were men. More than 90 per cent were white. About one-half of those participating were over 70 years of age; another 40 per cent were 50 to 69 years old. Thus, 90 per cent were between 50 and 90 years of age. Of 1,606 reactors, 71 per cent were men, of whom 90 per cent were 50 to 60 years of age. About 76 per cent of the total tested were reactors. Of 1,420 men tested, 80 per cent were reactors. Sixty-nine per cent of the 684 women tested reacted positively. Seventy-five per cent of the white population and 86 per cent of the nonwhite group were positive. The percentage of reactors (81.5) was highest among those ranging between the ages of 50 and 69. About 74 per cent of those between the ages of 70 and 89 reacted. Of 45 subjects over 90 years of age, 53.3 per cent reacted. It was concluded that tuberculosis remains a major problem in the aged population because of the high residual of infection. It was suggested that retesting of this age group every 10 years may provide information as to this residual infection. E. W.

The Tuberculin Reaction During Chemotherapy for Pulmonary Tuberculosis. Schwartz, S.: Dis. Chest **31**: 286, 1957.

Forty-nine adult male patients, most of whom had moderately advanced or far advanced pulmonary tuberculosis with cavity formation, were tested with first strength PPD intradermally before chemotherapy was administered. The ages of the patients varied from 20 to 60 years. Fifteen of the patients were Negroes and the rest were white. Skin-testing with PPD was repeated monthly for the first 4 months and then bimonthly for as long as one year after chemotherapy was started. Nine patients who did not react to first strength PPD, or had less than 5 mm. induration, were classified as hypoergic. A significant increase in size of reaction occurred predominantly in Negro patients under 50 years of age with far advanced tuberculosis. This change coincided with the period of resolution of the disease process and was present in the first or second month of treatment. This increase in reaction was most marked in the 9 hypoergic cases after treatment was started. Excluding this group of patients, a depression in the size of reaction occurred at the eighth and twelfth months of treatment. This depression occurred only in patients whose sputum changed from positive to negative. No significant differences

in response of the tuberculin reaction under chemotherapy could be determined between different chemotherapy regimens which consisted of mixtures of streptomycin plus PAS, streptomycin plus isoniazid, or isoniazid plus PAS. The significance of the change in size of tuberculin reaction and its relation to therapeutic response and tuberculin allergy is discussed in detail. E. W.

Effect of Possible Smog Irritants on Human Subjects. Sim, V. M., and Prattle, R. E.: J. A. M. A. **165**: 1908, 1957.

Healthy men were exposed to sulfur dioxide, sulfuric acid mist, various aldehydes, and other irritant substances which are believed to be present in smog. Experimental exposure to these substances was accomplished by two methods, one employing a mask and the other involving a chamber of sufficient size to accommodate many subjects simultaneously. Unexposed control subjects were also studied. The exposed men were observed closely throughout the exposure day and examined routinely on three succeeding days. No group was exposed more than twice in a single week. Test conditions were kept standardized throughout the entire 10-month period of the experiment.

The main effects of exposure to sulfur dioxide gas and sulfuric acid mist was an increase in airway resistance and the appearance of râles, rhinorrhea, and lacrimation. Long-lasting bronchitic symptoms developed in two subjects exposed to sulfuric acid mist. The addition of water vapor increased the mean particle size of the sulfuric acid mist and intensified its irritant effects. In another experiment, it was found that these acid compounds could be neutralized and their irritant effects abolished by adding ammonia gas to the sulfuric acid mist or magnesium oxide smoke to the sulfur dioxide atmosphere. Acrolein and crotonaldehyde were highly irritant, but formaldehyde was less irritant and acetaldehyde and its higher homologues were almost nonirritant. Since the concentration of sulfuric acid mist in atmospheric fog can be 3 times greater than that of sulfur dioxide, it appeared possible "that 4 ppm of sulfuric acid may have been present in the London fog of 1952, when the death rate from respiratory diseases rose to 5.7 times normal." M. C.

Auto-Immune Hemolytic Anemia Arrested by Removal of an Ovarian Teratoma: Review of the Literature and Report of a Case. Barry, K. G., and Crosby, W. H.: Ann. Int. Med. **47**: 1002, 1957.

The authors report a case of auto-immune hemolytic anemia of the type in which the formation of antibodies against the patient's own red cells appears to be related to the presence of a neoplasm (usually malignant). Other forms of the syndrome, often referred to as symptomatic auto-immune hemolytic anemia, may be associated with syphilis (paroxysmal cold hemoglobinuria), virus pneumonia, infectious mononucleosis, pregnancy, sarcoidosis, and Felty's syndrome. When the condition is associated with an ovarian teratoma, complete cure can be effected by removal of the tumor.

The authors describe such a case in a 26-year-old married nurse, on whom a diagnosis of sickle-cell anemia had been made and in whom repeated blood transfusions had been of little help. The blood picture, in addition to the sickle-cell trait, showed an intense spherocytosis. The spleen was markedly enlarged. Removal of an ovarian teratoma resulted in prompt recovery. H. F.